REMARKS/ARGUMENTS

Claims 14-16, 18-25 and 27-36 are pending in the application and have been finally rejected. Concurrent with this Amendment, Applicant has filed a Request for Continued Examination of the above claims. Applicant now amends claim 14 in a manner that it believes now places the claim in condition for allowance. The following remarks are submitted in support of the patentability of the pending claims, as amended.

Summary of Invention

The present invention is generally directed to a kit consisting of a single reaction vessel for each region of the DNA to be sequenced, where each reaction vessel contains sequencing primers specific for the sense strand and sequencing primers specific for the anti-sense strand of the region of DNA to be sequenced, together with specific non-region specific reagents. The sequencing primers specific for the sense strand and sequencing primers specific for the anti-sense strand are also labeled with a distinguishable detectable label.

The kits of the present invention are made possible as a result of methods and systems that have been previously been determined by the United States Patent and Trademark Office to be patentable (see, e.g., U.S. Patent Nos. 5,789,168; 5,830,657; 5,888,736; 6,083,699; and 6,214,555, to which patents the present application claims benefit of priority). The above-referenced patents describe and claim methods and systems for simultaneous PCR amplification and direct sequencing of multiple target DNAs, a methodology now commonly referred to as "CLIP sequencing." CLIP sequencing is essentially a patentable improvement on the coupled amplification and sequencing method of Ruano et al., in that CLIP sequencing (1) utilizes an improved engineered mutant of thermostable DNA polymerase that lacks 5′-3′ exonuclease activity that is capable of incorporating chain terminating dideoxynucleotides into an extending nucleic acid polymer at higher rates relative to the rate of incorporation of deoxynucleotides, thereby producing uniform band intensities, and (2) utilizes two inward-facing primers having distinguishable detectable labels to generate sequencing fragments for the sense and anti-sense DNA strands. Consequently, CLIP sequencing can be used to simultaneously amplify and sequencing substantially natural abundance DNA, and represents a novel methodology that enables and provides utility to kits that combine multiple primers, one specific for the sense strand of DNA and the other for the anti-sense strand of DNA, in a single reaction vessel, for

obtaining bi-directional sequence of a target region of DNA. The kits of the present invention are therefore useful for diagnostic sequencing of DNA samples, and reduce risk of error and contamination, increase the ease with which the procedure can be automated, and thereby potentially decrease the marginal costs in terms of equipment and labor for performing the test, as well as increase the reliability and accuracy of such tests.

Summary of Amendments

Applicant has amended claim 14 by deleting the term "optionally" before the clause reciting the non-region specific sequencing reagents, thereby requiring the presence of the non-region specific sequencing reagents in the kit.

Applicant has further specified that at least one chain terminating dideoxynucleotide triphosphate is present in a mole ratio to the corresponding deoxynucleotide triphosphate of from 1:50 to 1:1000 and that the thermally stable polymerase enzyme is capable of incorporating dideoxynucleotides into an extending nucleic acid polymer at a rate which is no less than 0.4 times the rate of incorporation of deoxynucleotides.

In view of the above amendments, Applicant has also amended claim 14 to delete the closed transitional term "consisting of" and replace it with the open-ended transitional term "comprising."

Remarks

Applicant notes, for the benefit of the examiner, that the claims of the present application now include substantially all of the limitations of issued U.S. Patent No. 6,214,555, to which the present application claims benefit of priority. The present application further includes the limitations that the recited primers are in a single reaction vessel, as well as the limitation that the sequencing primers are labeled with distinguishable detectable labels.

Applicant has already filed a terminal disclaimer in the present case, which effectively preempts any double-patenting issues that may arise between the present claims and the '555 patent.

In view of the above claim amendments and arguments presented above, Applicant submits that the rejections have been overcome and respectfully requests that the rejections be withdrawn and the claims allowed.

Respectfully submitted,

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